

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t902189982>

A SHORTER SYNTHESIS OF 5-THIO- α -D-GLUCOSE PENTAACETATE

M. M. A. Abd El-Rahman^a; Roy L. Whistler^a

^a Department of Biochemistry, Purdue University, Lafayette, Indiana

To cite this Article El-Rahman, M. M. A. Abd and Whistler, Roy L.(1973) 'A SHORTER SYNTHESIS OF 5-THIO- α -D-GLUCOSE PENTAACETATE', *Organic Preparations and Procedures International*, 5: 5, 245 – 249

To link to this Article: DOI: 10.1080/00304947309356849

URL: <http://dx.doi.org/10.1080/00304947309356849>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

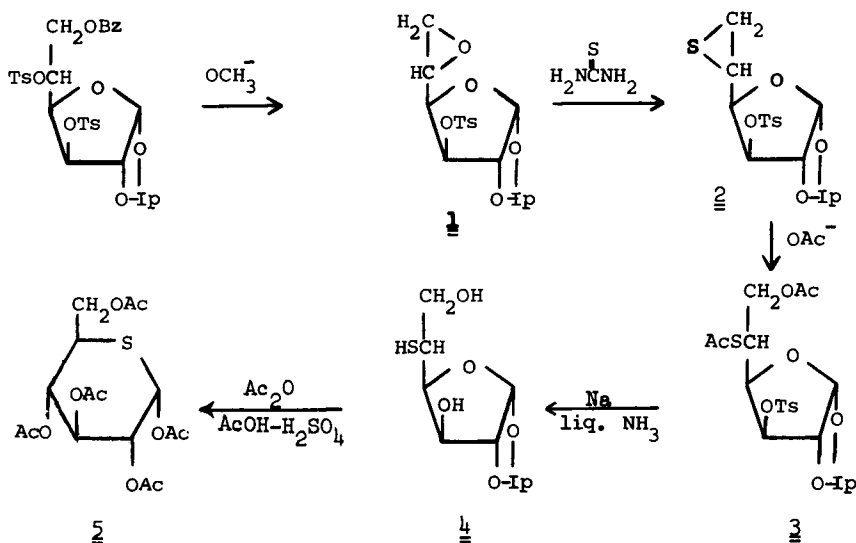
A SHORTER SYNTHESIS OF 5-THIO- α -D-GLUCOSE PENTAACETATE¹

M. M. A. Abd El-Rahman* and Roy L. Whistler**

Department of Biochemistry

Purdue University, Lafayette, Indiana 47907

We have been interested in the synthesis of sugars²⁻⁸ and nucleosides wherein sulfur replaces the normal ring oxygen atom. As part of a continuing work on the biochemistry of 5-thio-D-glucose,^{9,10} it was useful to synthesize the sugar analog by a shorter route. In this synthesis, we have reduced the number of steps and eliminated a time-consuming chromatographic separation.



M. M. A. ABD EL-RAHMAN AND R. L. WHISTLER

Compound 1 obtainable in 83% overall yield from 1,2-0-isopropylidene- α -D-glucofuranose, ^{11,12} was treated with thiourea ¹³ to produce the 5,6-dideoxy-5,6-epithio derivative 2 in 90% yield. Nucleophilic ring opening of 2 using fused potassium acetate in acetic acid and acetic anhydride gave crystalline 6-0-acetyl-5-S-acetyl-3-0-p-tolylsulphonyl-1,2-0-isopropylidene-5-thio- α -D-glucofuranose 3 in 95% yield. The IR spectrum exhibits characteristic absorption at 1740 cm^{-1} (0-acetyl) and 1685 cm^{-1} (S-acetyl). Reduction of 3 using sodium in liquid ammonia ¹⁴ yielded a 90% yield of 4, which on acetolysis produced 1,2,3,4,6-penta-0-acetyl-5-thio- α -D-glucopyranose 5. The overall yield of 5 from 6-0-benzoyl 1,2-0-isopropylidene- α -D-glucofuranose is 29%.

EXPERIMENTAL

Reactions were monitored by thin-layer chromatography (TLC) on silica gel G¹⁵ coated glass plates (5 x 13 cm), irrigated with benzene: ethyl acetate (4:1, v/v) or chloroform:methanol (4:1, v/v). Components were located in TLC by spraying with 5% sulphuric acid in ethanol and heating until permanent char spots were visible. Column chromatography used silica gel.¹⁶ Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter.

5,6-Anhydro-3-0-p-tolylsulphonyl-1,2-0-isopropylidene- β -l-idofuranose 1.

To a solution of 19 g. (0.03 mole) of 6-0-benzoyl-1,2-0-isopropylidene-3,5-di-0-tosyl- α -D-glucofuranose ¹⁷⁻¹⁹ in 200 ml. of dry chloroform cooled to -15° was added, under stirring, an ice-cold solution of sodium methoxide in methanol (2.0 g. of sodium dissolved in 35 ml. of methanol). The reaction mixture was worked up as described previously.¹⁴ The crude syrupy 5,6-anhydro compound 1 weighed 10.5 g. (98.1%) after removal of chloroform and distillation of methyl benzoate under reduced pressure, $[\alpha]_{\text{D}}^{22} -40.8^{\circ}$ (c 1.0 in CHCl_3).

5,6-Dideoxy-5,6-epithio-3-0-p-tolylsulphonyl-1,2-0-isopropylidene- α -D-glucofuranose 2.

To a solution of 1 (10.5 g.) in anhydrous methanol (130 ml.) was added thiourea (4.5 g.) and the mixture was stirred at 25°

A SHORTER SYNTHESIS OF 5-THIO- α -D-GLUCOSE PENTAACETATE

with the exclusion of moisture until the reaction was complete as indicated by TLC (about 60 hours). The solution was poured onto crushed ice and the solid mass obtained was washed with cold water and crystallized from ethanol to yield 9.8 g. (90%), mp 150-152°, $[\alpha]_D^{22}$ -135.9° (c 0.9 in CHCl_3).

Anal. Calcd. for $\text{C}_{16}\text{H}_{20}\text{O}_6\text{S}_2$: C, 51.61; H, 5.37; S, 17.20.

Found: C, 51.79; H, 5.45; S, 17.41.

6-O-Acetyl-5-S-acetyl-3-O-p-tolylsulphonyl-1,2-O-isopropylidene-5-thio- α -D-glucofuranose 3.— A mixture of 4 (9 g.), fused potassium acetate (6 g.), glacial acetic acid (20 ml.) and acetic anhydride (100 ml.) was refluxed for 20 hr. The reaction mixture was cooled and poured onto crushed ice whereby 3 crystallized. It was filtered, washed with ice-cold water and crystallized from ethanol to yield 10.8 g. (95%), mp 114°, $[\alpha]_D^{22}$ -31.0 (c 1.0 in CHCl_3). The infrared spectrum exhibited absorption peaks at 1740 (O-acetyl) and 1685 cm^{-1} (S-acetyl).

Anal. Calcd. for $\text{C}_{20}\text{H}_{26}\text{O}_9\text{S}_2$: C, 50.63; H, 5.48; S, 13.50.

Found: C, 50.52; H, 5.75; S, 13.32.

1,2,3,4,6-Penta-O-acetyl-5-thio- α -D-glucofuranose 5.— Compound 3 (0.96 g) in liquid ammonia (25 ml.) was reduced as previously described,¹⁴ to give an orange homogeneous syrup of 4 (0.41 g.). It was acetylyzed with 40 ml. of a mixture of acetic anhydride:acetic acid:sulphuric acid (70:30:1, v/v) on standing for 3 days. Anhydrous ether (50 ml.) was added followed by sodium acetate (1 g.), the mixture was then filtered and the residue was washed with ether. The combined solutions were co-evaporated with toluene to give a thick syrup which was chromatographed on silica gel column using ether:hexane (2:8, v/v) as eluent. Pure pentaacetate was collected as crystalline needles (0.21 g. 25.6%, mp. 102-103°, $[\alpha]_D^{22}$ +213 (c 1.0 in CHCl_3) lit.¹⁴ mp. 103°, $[\alpha]_D^{22}$ +213°, (c 1.35 in CHCl_3).

M. M. A. ABD EL-RAHMAN AND R. L. WHISTLER

5-Thio-D-glucose.— Compound 5 (24 g.; 0.77 mole) dissolved in 300 ml. of neat methanol was treated with 0.1 N sodium methoxide in methanol to pH 11. After 30 minutes TLC (chloroform:methanol; 4:1) indicated complete deacetylation and the solution was treated with IR 120 resin. The solution was filtered and the resin washed three times with 20 ml. portions of methanol. The filtrate was concentrated to a syrup under reduced pressure, dissolved in 20 ml. of hot methanol, cooled to 0° and 60 ml. of chloroform added. On cooling, 5-thio-D-glucose crystallized; yield 14 g. mp. 135–136°.

REFERENCES

*On leave of absence from Faculty of Science, Alexandria Univ., Egypt.

**To whom inquiries should be addressed.

1. This work was supported in part by a grant AM 15641 from the National Institute of Health, Journal Paper No. 5179 of the Purdue Agricultural Experiment Station.
2. R. L. Whistler, W. E. Dick, T. R. Ingle, R. M. Rowell and B. Urbas, *J. Org. Chem.*, 29, 3723 (1964).
3. E. J. Reist, D. E. Gueffroy and L. Goodman, *J. Amer. Chem. Soc.*, 86, 5668 (1964).
4. R. L. Whistler and R. M. Rowell, *J. Org. Chem.*, 29, 1259 (1964).
5. C. J. Clayton and N. A. Hughes, *Chem. Ind. (London)* 1795 (1962).
6. (a) J. C. P. Schwarz and K. C. Yule, *Proc. Chem. Soc.*, 417 (1961); (b) T. J. Adley and L. N. Owen, *ibid*, 418 (1961); (c) R. L. Whistler, M. S. Feather and D. L. Ingles, *J. Amer. Chem. Soc.*, 84, 122 (1962).
7. M. S. Feather and R. L. Whistler, *Tetrahedron Lett.*, 667 (1962).
8. C. W. Chiu and R. L. Whistler, *J. Org. Chem.*, 38, 832 (1973).
9. R. L. Whistler and W. C. Lake, *Biochemical J.*, 130, 919 (1972).
10. M. Pitts, R. L. Whistler, and M. M. A. Abd El-Rahman, unpublished

A SHORTER SYNTHESIS OF 5-THIO- α -D-GLUCOSE PENTAACETATE

results.

11. R. E. Gramera, A. Park and R. L. Whistler, *J. Org. Chem.*, 28, 3230 (1963).
12. A. S. Meyer and T. Reichstein, *Helv. Chim. Acta*, 29, 152 (1946).
13. L. D. Hall, L. Hough and R. A. Pritchard, *J. Chem. Soc.*, 1537 (1961).
14. U. G. Nayak and R. L. Whistler, *J. Org. Chem.*, 34, 100 (1969).
15. L. Merk Ag, Darmstadt, Germany, Distributors: Brinkman Instruments Inc., Westbury, N. Y. 11590.
16. J. T. Baker Chemical Co., Phillipsburg, N. J.
17. H. Ohle, *Ber.*, 57, 403 (1924).
18. E. J. Hedgley, Om Mérész and W. G. Overend, *J. Chem. Soc.*, (c), 893 (1967).
19. H. Ohle and E. Dickhäuser, *Ber.*, 58, 2593 (1925).

(Received July 5, 1973; in revised form August 13, 1973)